[0174] A fourth strategy for encoding and decoding bead identities is to use an intrinsic property of the magnetic beads such as their magnetization. The magnetic bead particles may be encoded with a varying magnetization (magnetite content) and detected via their differential response in a magnetic field. Spin valve detectors (explained below in the section entitled Detection) may be used to detect such magnetic beads and differentiate between populations of beads having different magnetization. Other detection methods may also be used.

[0175] The primary purpose of encoding a bead is to allow the identity of a probe attached to the bead to be subsequently determined. A similar result may be obtained by applying an encoding scheme to the probe itself instead of, or in addition to, encoding the bead. Many of the above encoding approaches may be applied to probes. For example, a probe can be color-coded, e.g., by attaching a fluorescent dye molecule or incorporating such molecules during synthesis of the probe. Labeled nucleic acid probes may conveniently be obtained by using one or more fluorescently labeled nucleotides in the synthesis procedure. One or more hybridization tags may be attached to or included in a probe. For example, where the probe is a DNA molecule, the probe may contain a portion that is substantially complementary to a target sequence and another portion that is substantially complementary to one or more decoding tags. As mentioned above, direct (on-bead) sequencing of a probe can also be used to identify the probe.

[0176] The field of combinatorial chemistry frequently involves synthesis of molecules on beads using a stepwise approach (e.g., split and pool synthesis). These methods may involve the use of encoding in order to allow a subsequent identification of the structure of the synthesized molecule. Similar encoding schemes may be used in the context of the present invention, particularly in situations where a probe is synthesized on the bead. Such encoding schemes are described, for example, in WO 98/53093 and references therein; Barnes, C. and Balasubramanian, S., Czarnik, A. W., "Recent developments in the encoding and deconvolution of combinatorial libraries", *Curr Opin Chem Biol.* (2000) Jun;4(3):346-50; Czarnik, "Encoding methods for combinatorial chemistry", *Curr Opin Chem Biol.* (1997) Jun;1(1):60-6; and Maclean, D. et al., "Encoded combinatorial chemistry: synthesis and screening of a library of highly functionalized pyrrolidines"*Proc Natl Acad Sci USA.* 1997 Apr 1;94(7):2805-10.

[0177] In general, in the schemes described above encoding of either the bead or the probe is sufficient to identify the bead (and thus the attached probe) or to identify the probe respectively. Thus if the bead is encoded no modification to the probe for encoding purposes is required. Conversely, if the probe is encoded, no independent encoding scheme for the bead is required, and the probe may be attached to an unmodified magnetic bead. An advantageous use of hybridization tags that may be used for assays involving nucleic acid hybridization (e.g., genotyping assays) involves modifications to both the bead and the probe.

[0178] According to this hybridization tag scheme populations of beads are encoded using any of the strategies described above (e.g., color-coding, magnetization, hybridization tags). A set of standard hybridization tags (e.g., oligos of 20 nucleotides in length) is selected to encode the probes. If hybridization tags are also used to encode the beads, a different standard set of hybridization tags should be used to encode the probes. The number of different tags can be arbitrarily large, depending on the number of different probes that are to be employed in the assay. The tags can be selected to interact (i.e., hybridize) minimally with each other and can be balanced with respect to properties such as melting temperature.

[0179] Probes whose sequence includes both (1) a sequence that is complementary to the sequence of a target to be detected by that probe and (2) the sequence of a hybridization tag assigned to that probe are prepared. Such probes may be, for example, approximately 40 nucleotides in length, where one 20 nucleotide stretch is a particular hybridization tag while a second 20 nucleotide stretch is intended to interrogate the sample (i.e., it is complementary to a target sequence of interest). The probes may also incorporate a linker sequence at the end to be attached to the bead. An oligo having a sequence complementary to one of the hybridization tags is coupled to an encoded population of beads. The probe having the complementary hybridization tag is then combined with that population of beads, and hybridization is allowed to occur between the bead-linked oligo and the complementary portion of the probe (the hybridization tag).

[0180] Beads (with associated probes attached by hybridization via the hybridization tag) from multiple populations are pooled prior to interrogation of the sample. Targets within the sample are labeled, e.g., with a fluorescent molecule different to any such molecule used to encode the beads. Hybridization between sample and probe is allowed to occur either prior to assembling the bead array or on-chip. After assembly of the array (and hybridization, if hybridization is performed on-chip), detection is performed. Following detection, decoding involves determining the identity of any beads with which the target has interacted (e.g., beads that have a target bound to their coupled probe). The bead is decoded using the decoding strategy appropriate to the way the bead was encoded. Decoding the identity of the bead reveals the identity of the hybridization tag whose complement was coupled to the bead. The identity of this hybridization tag in turn reveals the identity of the probe, including the identity of the sequence that was included in the probe in order to interrogate the sample. Thus the fact that the target interacted with (e.g., bound to) a particular probe is revealed.

[0181] In the context of a genotyping assay, this approach allows reformatting of the variable sequence of interest at the genomic region of interest to a standard hybridization tag. The power of this technique is that one can always use a pre-selected set of 20-mer hybridization tags with exceptional hybridization properties (e.g. no cross-interactions between them). The same bead populations are therefore usable experiment after experiment with an arbitrary choice of markers (sites) that one wishes to interrogate in the genome. All that is required is the synthesis of probes that include the complement of the marker and a hybridization tag whose complement is attached to a population of beads.

[0182] The foregoing approach is applicable to contexts other than genotyping and to biomolecules other than DNA. For example, RNA samples can be reformatted similarly. In addition, proteins can be reformatted with the same set of